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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,575	06/05/2006	Paul Wentworth	1361.027US2	3392

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THE SCRIPPS RESEARCH INSTITUTE
OFFICE OF PATENT COUNSEL, TPC-8
10550 NORTH TORREY PINES ROAD
LA JOLLA, CA 92037

EXAMINER	
ARCHIE, NINA	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
11/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,575	WENTWORTH ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23,25 and 29-47* is/are pending in the application.

4a) Of the above claim(s) *1-20,31 and 35-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21, 23, 25-26, 29-30, 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is responsive to Applicant's amendment and response filed on 7/22/2008 has been entered into the record. Claims 1-21, 23, 25-26, 29-47 are pending. Claim 21.

Objections/Rejections Withdrawn

2. In view of the Applicant's amendment and remark following objections are withdrawn.

a) Objection to claim 22, is withdrawn in light of in light of cancellation of the claim.

b) Rejections to claims 21, 23, 25, 29-30, and 33 under 35 U.S.C. 103(a) is withdrawn in light of applicant cancellation of claims (22) and in light of applicant's amendment thereto (claim 21).

c) Rejections to claims 21-34 under 35 U.S.C. 103(a) is withdrawn in light of applicant cancellation of claims (22) and in light of applicant's amendment thereto (claim 21).

d) Rejection to claims 21-34 under 35 U.S.C. 112, first paragraph, is withdrawn in light of applicant cancellation of claims (22), in light of applicant's amendment thereto (claim 21) and applicant's arguments.

e) Rejection of claims 21, 23-30 and 32-34 under 35 U.S.C. 112, first paragraph, is withdrawn in light of applicant cancellation of claims (22), in light of applicant's amendment thereto (claim 21).

f) Rejection of claims 21, and 27-28 under 35 U.S.C. 112, second paragraph, is withdrawn in light of applicant cancellation of claims (27-28).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Examiner interprets claim 21 as a method for treating bacterial infection via production of ozone in a mammal comprising administering to the mammal an anti-microbial composition consisting essentially of an antibody that can bind to a microbe, a sensitizer molecule that can generate singlet oxygen and a pharmaceutically acceptable carrier, wherein the sensitizer molecule is not conjugated to the antibody, wherein said composition yields the production of ozone.

3. Claims 21, 23, 25-26, 29-30, 32-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 21, 23, 25-26, 29-30, 32-34 are drawn to a method of treating bacterial infection comprising administering to the mammal an anti-microbial composition consisting essentially of an antibody that can bind to a microbe, a sensitizer molecule that can generate a singlet oxygen and a pharmaceutically acceptable carrier, wherein the sensitizer molecule is not conjugated to the antibody via production of ozone in a mammal.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude

that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

The claims are so broad that they encompass any method of treating every genus of bacterial infection to produce ozone production in a mammal; however applicants have not described such a method. The instant specification fails to provide a method where all bacterial infections will be treated to produce ozone in a mammal. The specification fails to teach that every type of microbe that can bind to any antibody within the claimed method. There is no teaching of an anti-microbial composition as set forth supra to treat bacterial infections associated with parasites, viruses, fungi, yeasts and bacteria with an to produce ozone in a mammal. The specification teaches the bactericidal activity of the antibody and source of singlet oxygen within an in vitro assay. Moreover, example IV teaches said activity towards Salmonella, wherein the inhibition of growth occurred during the in vitro portion. Additionally, as evidenced by Greenspan et al. (Nature Biotechnology 7: 936-937, 1999), defining epitopes is not as easy as it

seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Moreover, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows that the immunoepitopes that can elicit a protective immune response to a given pathogen can only be identified empirically. There is no written description of any method steps which teach such broadly claimed methods. There are no examples that teach the treatment of each and every type of microorganism using the product an anti-microbial composition as claimed. The claims fail to recite the necessary method steps. There are no data showing that the growth of bacteria will be inhibited or ameliorated in every microbial infection administering to a mammal using the product an anti-microbial composition as claimed. This demonstration is required for the skilled artisan to be able to use the claimed method for its intended purpose. The generic statements drawn to the method do not provide ample written description for the method.

As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. The possible structural variations are limitless to any class of bacterial infections that can be treated, and antibodies and microbes that can be used. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any specific examples of any type of bacterial infection treated with the product of an anti-microbial composition as claimed, the specification is void of any method of treating any type of bacterial infection to produce ozone production. The written description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will

hopefully ameliorate."). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention and the claims are rejected.

4. Claims 21, 23, 25-26, 29-30 and 32-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claim recites the phrase "via production of ozone in mammal". Although Applicant filed an explanation in the Applicants Arguments/Remarks on 7/22/2008, stating support for the recitation set forth supra, there is no support provided in the in the written description of the specification although applicant stated support in the explanation (see pg. 2, 2nd paragraph, pg. 13 last full paragraph, pg. 20 last full paragraph, pg. 22, 3rd paragraph). Therefore, it is apparent, that Applicants were not in possession of the claimed monoclonal antibody at the time of filing. Applicants pointing to the specification by page and line number where specific written description for the recitation set forth supra may resolve this issue. This is a new matter rejection.

5. Claims 21, 23, 25-26, 29-30 and 32-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabled for any method for treating bacterial infection via production of ozone comprising administering to the mammal an anti-microbial composition consisting essentially of an antibody that can bind to a microbe, a sensitizer

molecule that can generate singlet oxygen and a pharmaceutically acceptable carrier, wherein the sensitizer molecule is not conjugated to the antibody.

Enablement is considered in view of the *Wands* factors (MPEP 2164.01(a)).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims is very broad and the quantity of experimentation required is undue. The product being used to administer to a subject (human or otherwise) stated in claim 21, is overly broad. Claim 1 an antibody that can bind to any microbe and said antibody. Therefore it is hard for one skilled in the art to determine if the composition can be used in treating any type of bacterial infections in a mammal to yield the production of ozone. The quantity of experimentation required to practice the invention as claimed would require the de novo determination of accessible target sites, modes of delivery and formulations of the anti-microbial compositions to target appropriate cells

and/or tissues in any and/or all organisms/subjects, and further whereby treatment effects are provided for the claimed conditions. Since the specification fails to provide particular guidance for administering an anti-microbial composition comprising any antibody that can bind to any microbe to produce ozone in a mammal for treatment of any bacterial infection, it would require undue experimentation to practice the invention over the broad scope as presently claimed.

Nature of the invention/The existence of working examples.

The claims are drawn to method of treating bacterial infection via production of ozone comprising administering to the mammal an anti-microbial composition consisting essentially of an antibody that can bind to a microbe, a sensitizer molecule that can generate singlet oxygen and a pharmaceutically acceptable carrier, wherein the sensitizer molecule is not conjugated to the antibody, wherein said composition produces ozone in a mammal.

The state of the prior art is unpredictable with regard to microbial infection treatments comprising an antimicrobial composition as set forth supra. The state of the art teaches that Hasan et al teach a method of treating a subject, for a disorder characterized by the presence of an unwanted organism such as Salmonella, comprising: administering to the subject a conjugate comprising a polylysine backbone to which is coupled a targeting moiety and a porphyrin photosensitizer such as a hematoporphyrins (see claims, section “Phostosensitizers” Hasan et al US Patent 7,268,155 September 2007). The art indicates that Goers et al teach an antibody-therapeutic agent conjugate, comprising: a therapeutic agent capable of acting as a photothermolytic agent, as a photosensitizer to mediate cytotoxic effects nearby cells are mediated through the generation of singlet oxygen molecules and oxygen free radicals (see claims abstract, Section 3 Summary of Invention paragraphs 1-4, see section 7 see Goers et al WO 1986/001720 March 1986 in its entirety). The art indicates that Wentworth et al teach that antibodies to convert molecular oxygen into hydrogen

peroxide, thereby effectively linking recognition and killing events (see abstract). Wentworth et al teach that irradiation of antibodies with visible light in the presence of a known photosensitizer of ozone in aqueous solutions, hematoporphyrin, leads to hydrogen peroxide formation (see column 2 paragraph 2). Thus Wentworth et al teach reactive oxygen species is hydrogen peroxide.

The art indicates ozone in the body may have a protective role against pathogenic invaders. The art indicates reactive oxygen species (ROS) (hyroxyl radical, nitric oxide, and hydrogen peroxide) produced by immune system cells during infectious processes. The art indicates the crucial role of ozone in the task of staving off invading microorganisms had not been as fully explained in under-publicized article with momentous implications (Wentworth et al 2002) documented that ozone is indeed produced in the body in the context of immune function. The art indicates antibodies, provided with appropriate starting materials, are capable of creating singlet oxygen, a most powerful oxidant. The art indicates ozone in combination with hydrogen peroxide, could account for the inactivation of 95% of Escherichia coli bacteria, ozone thus becomes a pivotal factor for fighting microorganisms. The art indicates that ozone functions as a signaling agent by stimulating production of nuclear factor kappa B, interleukin 6, and tumor necrosis factor a. The art indicates ozone is a strong bactericide needing only a few micrograms per milliliter for measurable action at a concentration of 1 mg/liter H2O, ozone rapidly inactivates bacteria (See Sunnen pgs. 1-4 Sunnen see Gerald. Ozonics International Copyright 2005 in its entirety). The art indicates a partial list of organisms susceptible to ozone inactivation includes both aerobic and anaerobic bacteria. The art indicates while exogenously applied ozone has received total investigative focus, little or no attention has been paid to endogenously generated ozone. The art indicates ozone has been seen as a molecule capable of inducing the formation of reactive oxygen species but not as a molecule specifically produced by the body to fight infection and ozone in the task of staving off invading microorganisms and not as a molecule specifically produced by the body to fight infections (See Sunnen pgs 1-4). The art indicates research is compellingly needed to understand the deeper mechanisms of ozone and nitric oxide formation in the immune

system so that novel antimicrobial therapies may be recruited to respond to the world's increasingly urgent public health needs (See Sunnen pgs 1-4). The art has not shown any anti-microbial composition consisting essentially of an antibody that can bind to a microbe, a sensitizer molecule that can generate singlet oxygen and a pharmaceutically acceptable carrier, wherein said composition produces ozone in a mammal for treating bacterial infection. For the reasons set forth supra, the state of the art is unpredictable with regard to treating any bacterial infection.

Guidance in the specification. The specification discloses Examples of antibodies that have the capacity to destroy antigens and Microbiocidal action against Salmonella typhimurium. The specification teaches the bactericidal activity of the antibody and source of singlet oxygen within an in vitro assay. Moreover, example IV teaches said activity towards Salmonella, wherein the inhibition of growth occurred during the in vitro portion (see pp. 45-88). The specification does not give an example of an antimicrobial composition to treat bacterial infections. The examples disclose in the specification only contemplate the claimed invention. The specification provides little guidance regarding how the antimicrobial composition as set forth supra is effective when treating bacterial infections and further more how the anti-microbial composition as claimed will produce ozone in a mammal for treating a bacterial infection. Therefore one skilled in the art would not accept on its face the examples given in the specification as being correlative or representative of the successful treatment in any mammal by production of ozone. The specification as filed fails to provide particular guidance which resolves the known unpredictability in the art associated with effects provided upon administration via any route.

In conclusion, the claimed inventions are not enabled for any method for treating bacterial infection via production of ozone comprising administering to the mammal an anti-microbial composition consisting essentially of an antibody that can bind to a microbe, a sensitizer molecule that can generate singlet oxygen and a pharmaceutically acceptable carrier, wherein the sensitizer molecule is not conjugated to the antibody. Furthermore, the specification does not give an example of an antimicrobial composition

to treat bacterial infections. The examples disclose in the specification only contemplate the claimed invention. The product being used to administer to a mammal stated in claim 21, is overly broad. The state of the art is unpredictable to administer antimicrobial composition to treat bacterial infections and produce ozone in a mammal. As a result, for the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed methods.

Status of the Claims

6. No claims are allowed.

Claims 21, 23, 25-26, 29-30 and 32-34 are rejected.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina Archie
Examiner
Art Unit 1645

/Nina A Archie/
Examiner, Art Unit 1645
/N. A. A./
Examiner, Art Unit 1645

/Mark Navarro/

Primary Examiner, Art Unit 1645